Amendments to the Specification:

Please amend the paragraph beginning at page 1, line 6 as follows:

This application is the National Stage of International Application No. PCT/US2004/001461, filed on January 21, 2004, which claims the benefit under 35 U.S.C. § 119 of German Patent No. 103 02 421.2, filed on January 21, 2003. The ~~disclosure~~ disclosures of the above ~~application is hereby~~ applications are incorporated herein by reference in ~~its~~ their entirety.

Please add the following new paragraphs after the paragraph ending at page 6, line 12:

List of other embodiments:

Embodiment 1. A double-stranded ribonucleic acid (dsRNA) having a strand S1 which is complementary at least in segments to a target gene (the antisense strand), a strand S2 which is at least substantially complementary to the strand S1 (the sense strand), wherein the dsRNA is capable of inhibiting the expression of the target gene upon introduction into a cell expressing said target gene, and wherein at least one lipophilic group is linked only to the strand S1, or only to the strand S2.

Embodiment 2. The dsRNA of embodiment 1, wherein the link between the lipophilic group and the dsRNA strand is a covalent bond.

Embodiment 3. The dsRNA of embodiment 2, wherein the lipophilic group is covalently attached to a 5'-end of the strand S1 or a 5'-end of the strand S2.

Embodiment 4. The dsRNA of embodiment 2, wherein the linkage between the lipophilic group and the dsRNA strand comprises a phosphodiester group.

Embodiment 5. The dsRNA of embodiment 2, wherein the linkage between the lipophilic group and the dsRNA strand does not comprise a phosphodiester group.

Embodiment 6. The dsRNA of embodiment 3, wherein the lipophilic group is covalently attached to the 5'-end of the strand S1.

Embodiment 7. The dsRNA of embodiment 3, wherein the lipophilic group is covalently attached to the 5'-end of the strand S2.

Embodiment 8. The dsRNA of embodiment 1, wherein the strand S1 comprises a 3'-end and a 5'-end, and wherein the 3'-end has a nucleotide overhang of 1 to 4 nucleotides.

Embodiment 9. The dsRNA of embodiment 8, wherein the nucleotide overhang consists of 1 or 2 nucleotides.

Embodiment 10. The dsRNA of embodiment 1, wherein the dsRNA is between 16 and 30 nucleotides in length.

Embodiment 11. The dsRNA of embodiment 1, wherein the dsRNA is between 16 and 25 nucleotides in length.

Embodiment 12. The dsRNA of embodiment 1, wherein the dsRNA is between 20 and 25 nucleotides in length.

Embodiment 13. The dsRNA of embodiment any of the preceding embodiments, wherein the lipophilic group is selected from the group consisting of an aromatic, aliphatic or alicyclic moiety, or a combination thereof.

Embodiment 14. The dsRNA of embodiment 13, wherein the lipophilic group is a steroid or a branched aliphatic hydrocarbon, or a combination thereof.

Embodiment 15. The dsRNA of embodiment 14, wherein the lipophilic group is a sterol.

Embodiment 16. The dsRNA of embodiment 15, wherein the sterol is cholesterol or a cholesterol derivative.

Embodiment 17. The dsRNA of embodiment 16, wherein the lipophilic group is cholesteryl (6-hydroxyhexyl) carbamate

Embodiment 18. The dsRNA of embodiment 13, wherein the lipophilic group is 12-hydroxydodecanoic acid bisdecylamide.

Embodiment 19. The dsRNA of embodiment 1, wherein the target gene is endogenous to the cell.

Embodiment 20. The dsRNA of embodiment 1, wherein the target gene is exogenous to the cell.

Embodiment 21. The dsRNA of embodiment 20, wherein the target gene is a viral gene.

Embodiment 22. The dsRNA of embodiment 21, wherein the viral gene is from a (+) strand RNA virus

Embodiment 23. The dsRNA of embodiment 22, wherein the (+) strand RNA virus is a Hepatitis C Virus.

Embodiment 24. The dsRNA of embodiment 23, wherein the target gene is at least a portion of a 3'-untranslated region (3'-UTR) of a Hepatitis C Virus.

Embodiment 25. The dsRNA of embodiment 1, wherein the lipophilic group has a $\log K_{ow}$ exceeding 1.

Embodiment 26. The dsRNA of embodiment 1, wherein the lipophilic group has a $\log K_{ow}$ exceeding 1.5.

Embodiment 27. The dsRNA of embodiment 1, wherein the lipophilic group has a $\log K_{ow}$ exceeding 2.

Embodiment 28. The dsRNA of embodiment 1, wherein the lipophilic group has a $\log K_{ow}$ exceeding 3.

Embodiment 29. The dsRNA of embodiment 1, wherein the lipophilic group has a $\log K_{ow}$ exceeding 5.

Embodiment 30. A pharmaceutical composition for inhibiting the expression of a target gene in a mammal, comprising:

a. a double-stranded ribonucleic acid (dsRNA) having a strand S1 which is complementary at least in segments to a target gene (the antisense strand), a strand S2 which is at least substantially complementary to the strand S1 (the sense strand), wherein the dsRNA is capable of inhibiting the expression of the target gene upon introduction into a cell expressing said target gene, and wherein at least one lipophilic group is linked only to the strand S1, or only to the strand S2; and

b. a pharmaceutically acceptable carrier.

Embodiment 31. The pharmaceutical composition of embodiment 30, wherein the link between the lipophilic group and the dsRNA strand is a covalent bond.

Embodiment 32. The pharmaceutical composition of embodiment 31, wherein the lipophilic group is covalently attached to a 5'-end of the strand S1 or a 5'-end of the strand S2.

Embodiment 33. The pharmaceutical composition of embodiment 31, wherein the linkage between the lipophilic group and the dsRNA strand comprises a phosphodiester group.

Embodiment 34. The pharmaceutical composition of embodiment 31, wherein the linkage between the lipophilic group and the dsRNA strand does not comprise a phosphodiester group.

Embodiment 35. The pharmaceutical composition of embodiment 32, wherein the lipophilic group is covalently attached to the 5'-end of the strand S1.

Embodiment 36. The pharmaceutical composition of embodiment 32, wherein the lipophilic group is covalently attached to the 5'-end of the strand S2.

Embodiment 37. The pharmaceutical composition of embodiment 30, wherein the strand S1 comprises a 3'-end and a 5'-end, and wherein the 3'-end has a nucleotide overhang of 1 to 4 nucleotides.

Embodiment 38. The pharmaceutical composition of embodiment 37, wherein the nucleotide overhang consists of 1 or 2 nucleotides.

Embodiment 39. The pharmaceutical composition of embodiment 30, wherein the dsRNA is between 16 and 30 nucleotides in length.

Embodiment 40. The pharmaceutical composition of embodiment 30, wherein the dsRNA is between 16 and 25 nucleotides in length.

Embodiment 41. The pharmaceutical composition of embodiment 30, wherein the dsRNA is between 20 and 25 nucleotides in length.

Embodiment 42. The pharmaceutical composition of embodiment 30, wherein the lipophilic group is selected from the group consisting of an aromatic, aliphatic or alicyclic moiety, or a combination thereof.

Embodiment 43. The pharmaceutical composition of embodiment 42, wherein the lipophilic group is a steroid or a branched aliphatic hydrocarbon, or a combination thereof.

Embodiment 44. The pharmaceutical composition of embodiment 43, wherein the lipophilic group is a sterol.

Embodiment 45. The pharmaceutical composition of embodiment 44, wherein the lipophilic group is cholesterol or a cholesterol derivative.

Embodiment 46. The pharmaceutical composition of embodiment 45, wherein the lipophilic group is cholesteryl (6-hydroxyhexyl) carbamate.

Embodiment 47. The pharmaceutical composition of embodiment 43, wherein the lipophilic group is 12-hydroxydodecanoic acid bisdecylamide.

Embodiment 48. The pharmaceutical composition of embodiment 30, wherein the target gene is endogenous to the cell.

Embodiment 49. The pharmaceutical composition of embodiment 30, wherein the target gene is exogenous to the cell.

Embodiment 50. The pharmaceutical composition of embodiment 49, wherein the target gene is a viral gene.

Embodiment 51. The pharmaceutical composition of embodiment 50, wherein the viral gene is from a (+) strand RNA virus

Embodiment 52. The pharmaceutical composition of embodiment 51, wherein the (+) strand RNA virus is a Hepatitis C Virus.

Embodiment 53. The pharmaceutical composition of embodiment 52, wherein the target gene is at least a portion of a 3'-untranslated region (3'-UTR) of a Hepatitis C Virus.

Embodiment 54. The pharmaceutical composition of embodiment 30, wherein the lipophilic group has a $\log K_{ow}$ exceeding 1.

Embodiment 55. The pharmaceutical composition of embodiment 30, wherein the lipophilic group has a $\log K_{ow}$ exceeding 1.5.

Embodiment 56. The pharmaceutical composition of embodiment 30, wherein the lipophilic group has a $\log K_{ow}$ exceeding 2.

Embodiment 57. The pharmaceutical composition of embodiment 30, wherein the lipophilic group has a $\log K_{ow}$ exceeding 3.

Embodiment 58. The pharmaceutical composition of embodiment 30, wherein the lipophilic group has a $\log K_{ow}$ exceeding 5.

Embodiment 59. The pharmaceutical composition of embodiment 30, wherein the pharmaceutically acceptable carrier is an aqueous solution.

Embodiment 60. The pharmaceutical composition of embodiment 58, wherein the pharmaceutically acceptable carrier does not contain an agent that mediates the uptake of the dsRNA into a cell.

Embodiment 61. A method for inhibiting the expression of a target gene in a mammal, which comprises administering a pharmaceutical composition comprising a double-stranded ribonucleic acid (dsRNA) and a pharmaceutically acceptable carrier, wherein the dsRNA comprises a strand S1 which is complementary at least in segments to a target gene (the antisense strand), a strand S2 which is at least substantially complementary to the strand S1 (the sense strand), wherein the dsRNA is capable of inhibiting the expression of the target gene upon introduction into a cell expressing said target gene, and wherein at least one lipophilic group is linked only to the strand S1, or only to the strand S2.

Embodiment 62. The method of embodiment 61, wherein the link between the lipophilic group and the dsRNA strand is a covalent bond.

Embodiment 63. The method of embodiment 62, wherein the lipophilic group is covalently attached to a 5'-end of the strand S1 or a 5'-end of the strand S2.

Embodiment 64. The method of embodiment 62, wherein the linkage between the lipophilic group and the dsRNA strand comprises a phosphodiester group.

Embodiment 65. The method of embodiment 62, wherein the linkage between the lipophilic group and the dsRNA strand does not comprise a phosphodiester group.

Embodiment 66. The method of embodiment 63, wherein the lipophilic group is covalently attached to the 5'-end of the strand S1.

Embodiment 67. The method of embodiment 63, wherein the lipophilic group is covalently attached to the 5'-end of the strand S2.

Embodiment 68. The method of embodiment 61, wherein the strand S1 comprises a 3'-end and a 5'-end, and wherein the 3'-end has a nucleotide overhang of 1 to 4 nucleotides.

Embodiment 69. The method of embodiment 68, wherein the nucleotide overhang consists of 1 or 2 nucleotides.

Embodiment 70. The method of embodiment 61, wherein the dsRNA is between 16 and 30 nucleotides in length.

Embodiment 71. The method of embodiment 61, wherein the dsRNA is between 16 and 25 nucleotides in length.

Embodiment 72. The method of embodiment 61, wherein the dsRNA is between 20 and 25 nucleotides in length.

Embodiment 73. The method of embodiment 61, wherein the lipophilic group is selected from the group consisting of an aromatic, aliphatic or alicyclic moiety, or a combination thereof.

Embodiment 74. The method of embodiment 61, wherein the lipophilic group is a steroid or a branched aliphatic hydrocarbon, or a combination thereof.

Embodiment 75. The method of embodiment 74, wherein the lipophilic group is a sterol.

Embodiment 76. The method of embodiment 75, wherein the lipophilic group is cholesterol or a cholesterol derivative.

Embodiment 77. The method of embodiment 76, wherein the lipophilic group is cholesteryl (6-hydroxyhexyl) carbamate.

Embodiment 78. The method of embodiment 74, wherein the lipophilic group is 12-hydroxydodecanoic acid bisdecylamide.

Embodiment 79. The method of embodiment 61, wherein the target gene is endogenous to the cell.

Embodiment 80. The method of embodiment 61, wherein the target gene is exogenous to the cell.

Embodiment 81. The method of embodiment 80, wherein the target gene is a viral gene.

Embodiment 82. The method of embodiment 81, wherein the viral gene is from a (+) strand RNA virus

Embodiment 83. The method of embodiment 82, wherein the (+) strand RNA virus is a Hepatitis C Virus.

Embodiment 84. The method of embodiment 83, wherein the target gene is at least a portion of a 3'-untranslated region (3'-UTR) of a Hepatitis C Virus.

Embodiment 85. The method of embodiment 61, wherein the lipophilic group has a $\log K_{ow}$ exceeding 1.

Embodiment 86. The method of embodiment 61, wherein the lipophilic group has a $\log K_{ow}$ exceeding 1.5.

Embodiment 87. The method of embodiment 61, wherein the lipophilic group has a $\log K_{ow}$ exceeding 2.

Embodiment 88. The method of embodiment 61, wherein the lipophilic group has a $\log K_{ow}$ exceeding 3.

Embodiment 89. The method of embodiment 61, wherein the lipophilic group has a $\log K_{ow}$ exceeding 5.

Embodiment 90. A method for making a double-stranded ribonucleic acid (dsRNA), comprising the steps of:

a. preparing a first RNA strand S1 and a second RNA strand S2, wherein strand S1 is complementary at least in segments to a target gene, strand S2 is at least substantially complementary to the strand S1, wherein the dsRNA is capable of inhibiting the expression of the target gene upon introduction into a cell expressing said target gene, and wherein at least one lipophilic group is linked only to the strand S1, or only to the strand S2; and

b. mixing strand S1 and strand S2 to form a dsRNA.

Embodiment 91. The method of embodiment 90, wherein the step of preparing the RNA strands comprises solid-phase synthesis in a 3' to 5' direction.

Embodiment 92. The method of embodiment 91, further comprising the step of attaching the lipophilic group to strand S1 or strand S2, wherein the step comprises reacting a lipophilic molecule having a phosphoramidite group with a 5'-hydroxyl group of strand S1 or strand S2.

Embodiment 93. The method of embodiment 92, wherein the phosphoramidite group on the lipophilic molecule is formed by phosphitylation of a hydroxy group.

Embodiment 94. The method of embodiment 92, wherein the lipophilic molecule having a phosphoramidite group is formed by converting a cholesteryl chloroformate into an amide.

Embodiment 95. The method of embodiment 92, wherein the lipophilic molecule having a phosphoramidite group is formed by reacting a 12-hydroxylauric acid with a di-n-decylamine to form an amide.

Embodiment 96. The method of embodiment 92, wherein the lipophilic molecule having a phosphoramidite group is cholesteryl N-[6-(2-cyanoethoxy)-N,N-diisopropylaminophosphanyloxy]-hexyl carbamate or 12-[(2-cyanoethoxy) -N,N-diisopropylamino-phosphanyloxy]dodecanoic acid bisdecylamide.

Embodiment 97. The method of embodiment 92, wherein the lipophilic group has a $\log K_{ow}$ exceeding 1.

Embodiment 98. The method of embodiment 92, wherein the lipophilic group has a $\log K_{ow}$ exceeding 1.5.

Embodiment 99. The method of embodiment 92, wherein the lipophilic group has a $\log K_{ow}$ exceeding 2.

Embodiment 100. The method of embodiment 92, wherein the lipophilic group has a $\log K_{ow}$ exceeding 3.

Embodiment 101. The method of embodiment 92, wherein the lipophilic group has a $\log K_{ow}$ exceeding 5.